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Kidney International, Vol. 45 (1994), pp. 1163–1169

Continuous ambulatory peritoneal dialysis and hemodialysis: Comparison of patient mortality with adjustment for comorbid conditions

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Continuous ambulatory peritoneal dialysis and hemodialysis: Comparison of patient mortality with adjustment for comorbid conditions. A historical prospective national sample of 1,725 diabetic and 2,411 non-diabetic Medicare end-stage renal disease (ESRD) patients incident from 1986 to 1987 was analyzed for the mortality of patients selected to receive continuous ambulatory peritoneal dialysis (CAPD) or hemodialysis (HD) with adjustment for patient characteristics, including the presence of comorbid conditions at onset of ESRD. Cox proportional hazards analyses were used to compare the mortality of CAPD and HD patients. Patients were followed from 30 days following onset of ESRD until two to four years post-onset. No statistically significant difference in relative mortality risk (RR) was found among non-diabetic patients selected for CAPD compared to HD (RR = 0.84 for CAPD versus HD, $P = 0.25$), while evidence of higher adjusted mortality for CAPD compared to HD was found among diabetic patients (RR = 1.26, $P = 0.03$). Mortality analyses adjusted for pre-treatment risk factors suggest that CAPD and HD provide incident non-diabetic ESRD patients with similar expected survival outcomes. Evidence that increased mortality was associated with CAPD among diabetic patients, particularly among elderly patients, suggests the need for further controlled studies of mortality among CAPD patients with diabetes.

During 1990 the number of people beginning treatment for end-stage kidney failure under the Medicare ESRD program in the U.S. was over 45,000, a number that increased by 8 to 11% per year between 1986 and 1990 [1]. For the increasing numbers of ESRD patients requiring maintenance therapy each year, treatment with renal transplantation has become limited by the availability of organs, resulting in waiting times for transplants typically exceeding one year. The two primary dialysis treatment options include hemodialysis and continuous ambulatory peritoneal dialysis (CAPD), which combined were used to treat 92% of dialysis patients and 68% of ESRD patients prevalent in 1990 [1]. The selection of an appropriate dialytic therapy is influenced by many factors, including the expected survival outcome for each patient, given individual characteristics and an associated level of pre-treatment mortality risk.

Received for publication April 2, 1993
and in revised form October 28, 1993
Accepted for publication October 28, 1993

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Several previous studies of incident (new) ESRD patients have demonstrated that the process of selecting dialysis modality is not random [2–6]. Overall patterns in the selection of patients to CAPD as opposed to HD have revealed differences in the level of comorbidity between patients receiving CAPD and those receiving HD, with statistical adjustment for age, race, and diabetes [2]. Further, many of the individual comorbid conditions shown to influence selection of therapy were associated with increased mortality in a prior analysis of HD patients [7]. Studies that compare patient outcomes by treatment modality without adjusting for comorbidity may incorrectly attribute differences in mortality to differences in the quality of treatment.

This study compares patient survival outcomes for a large national randomly selected sample of 1986 to 1987 incident ESRD patients receiving CAPD or HD at thirty days following onset of ESRD. All comparisons of patient mortality and survival between CAPD and HD have been adjusted for an extensive set of patient risk factors, including the presence of comorbid conditions within ten years prior to reaching end-stage kidney failure.

Methods

Data collection

The origin of most of the data used in these analyses is the Case Mix Severity Special Study of the United States Renal Data System (USRDS). These data were abstracted from patient medical records by the 18 ESRD Networks under contract with the Health Care Financing Administration (HCFA) using a data collection form developed and tested by the USRDS Coordinating Center, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and HCFA [8]. The data were abstracted during 1989 for a sample of 4,892 patients who started dialysis therapy for ESRD during 1986 to 1987. All patients in the study were Medicare-entitled for dialysis services within 90 days following onset of ESRD. Patients were selected using a national randomized two-stage cluster sampling process. ESRD patients incident in the U.S. during 1986 to 1987 were selected at random (from 291 dialysis units also selected at random) according to the last two digits of their social security

numbers. To facilitate data abstraction, the sample design was limited geographically to those dialysis units within one day's travel of one of 18 ESRD Network Offices in the United States.

Among the data collected were patient identifiers, information on health insurance, the presence or absence of a variety of comorbid conditions within ten years prior to diagnosis of ESRD, physical characteristics (patient height, weight, nutritional status, blood pressure) measured within two to six weeks of ESRD onset, dialysis treatment modality, prescribed dose of dialysis, date of transplant (for censoring), psychosocial status at onset of ESRD, and ESRD-related laboratory data. A copy of the data abstraction form used to collect data for this study was published in Appendix B of the USRDS 1992 Annual Data Report [4].

The data collected on the abstraction form were supplemented with data from the USRDS database, which contains longitudinal data on all Medicare ESRD patients in the United States from 1977 to the present [8]. Most of these data are derived from the HCFA Program Management and Medical Information System [8]. The supplemental data used in this analysis, including the date of first dialysis service and the date and type of changes in dialysis treatment modality, were not collected during data abstraction. USRDS data were based on a March 31, 1991 update of HCFA file sources, which were used to determine survival and transplant status as of April 1, 1990.

Analytical methods

This analysis compared survival outcomes for new ESRD patients selected to the CAPD and HD patient groups after adjusting for differences in socio-demographic factors (age, sex, race, primary cause of ESRD) and other indicators of case mix severity (comorbid conditions before onset of ESRD). Patients were assigned to a modality group based on the method of treatment they were receiving at one month after reported onset of ESRD. Modality classifications included CAPD, continuous cycling peritoneal dialysis (CCPD), and hemodialysis (HD), performed in-center or at home. Patients receiving intermittent peritoneal dialysis, dialysis of an unknown type, or who had a functioning graft at one month post-ESRD were excluded from this study. Patients less than 15 years old at onset of ESRD were also excluded from these analyses since selection of a treatment modality for younger children involves many considerations that do not apply to older patients.

Given the broad clinical differences between diabetic and non-diabetic patients, analyses of patient mortality were performed separately according to the presence of diabetes. Two sources were used to classify patients as diabetic: (1) the USRDS database, which indicated the primary cause of ESRD as diabetic nephropathy; and (2) the Case Mix Severity Study data collection form, which was used to indicate a history of diabetes within ten years of onset of ESRD. All diabetic patients were combined into a single category, regardless of the type or duration of diabetes prior to onset of ESRD.

The expected mortality effects of differences in selection according to patient characteristics, specifically age, race, and diagnosis, were evaluated using results from previous research. This was done by weighting previous estimates of the risk ratio for each characteristic by the proportion of patients with that characteristic in the current study. The result was expressed for CAPD relative to HD. For example, diabetic patients, selected with greater frequency for CAPD (45.5% DM) than for HD (40.9% DM) in the current study, have been shown to be at higher risk of death [9–12] than non-diabetic patients (RR = 1.9), yielding slightly higher expected mortality for patients selected for CAPD, independent of other factors: [0.455*1.9 + 0.545*1]/[0.409*1.9 + 0.591*1], or RR = 1.03.

Analyses of patient mortality adjusted for patient characteristics and comorbid conditions employed Cox proportional hazards regression techniques [13]. To allow for a delay in the reporting of death data, follow-up was stopped on April 1, 1990, yielding a follow-up period of 2.25 to 4.25 years for each patient. Patients were censored (that is, removed from the analysis) 30 days after the first change in dialysis modality (modality history model) to attribute time at risk and any deaths during the initial 30 days following the first modality change to the original modality. The dependent variable used in proportional hazards analyses measured the time in days from onset of ESRD to the earliest of death, transplant, 30 days after the first modality change, or April 1, 1990. Only patients surviving at least 90 days following onset of ESRD were considered.

The primary Cox proportional hazards model included age at onset of ESRD, race (black, white, other), gender, modality type (HD, CAPD, CCPD), and several indicators of comorbidity at time of ESRD. The measured comorbid conditions included the presence or absence of coronary heart disease, congestive heart failure, cerebrovascular accident, peripheral vascular disease, neoplasm, smoking status, obesity, and inability to ambulate, eat, or transfer. A comprehensive list of the 25 individual comorbid conditions for which information was collected was reported in a previous analysis [2]. Other indicators of patient condition included serum albumin, modeled as a series of binary variables (0–2.4, 2.5–2.9, 3.0–3.4, 3.5–3.9, and $\geq$4.0 g/dl) to allow for non-linear effects of serum albumin on mortality, and systolic blood pressure ($<$120, 120–159, 160–199, and $\geq$200 mm Hg).

An age-by-modality interaction term was also included in the primary model to consider the hypothesis that comparisons of mortality between CAPD and HD vary by age [3]. In defining this interaction term, the mean age of all HD patients was subtracted from the age of each patient to allow the relative mortality risk for CAPD versus HD to be evaluated for the average aged patient. Similarly, an age-by-race interaction term was included in the model to adjust for the effect of age on mortality comparisons by race, since lower mortality among blacks relative to whites becomes accentuated as age increases [8]. Other covariates included pre-dialysis blood urea nitrogen (BUN) and creatinine values.

For patients lacking information for one or more covariates, numeric variables (such as, serum albumin) with missing values were set to the mean value across all non-missing observations in each diabetes subgroup, while categorical measures of comorbidity with missing values were set to zero (such as, comorbid condition not present). This was done to avoid the exclusion of these patients from the proportional hazards model due to small amounts of missing data. A generic "missing case mix data" variable was then defined to identify those patients lacking information for one or more covariates and was included in the model to account for potentially different mortality among subjects with missing data.

Stratified Cox proportional hazards models were used to

Table 1. Incident Medicare ESRD patient characteristics for CAPD and HD, 1986 to 1987[a]

Patient characteristic	HD (N = 3,376)	CAPD (N = 681)
Age *mean*	58.7	53.7
Black %	36.7	27.0
Female %	48.1	46.3
Diabetes %		
Primary Dx	28.1	36.4
Any prior Hx[b]	40.9	45.5

[a] Patients surviving <90 days were excluded
[b] Includes patients with diabetes as primary Dx in previous row

generate survival estimates for CAPD and HD, separately for diabetic and non-diabetic patients. Adjusted survival curves were calculated for CAPD and HD patients at the mean value for each of the patient covariates, for each diabetes subgroup. Survival estimates were therefore adjusted for the distribution of patient characteristics and comorbid conditions specific to diabetic and non-diabetic patients. To test the assumption of proportionality between the hazard functions for CAPD and HD, several tests were employed: (1) stratified adjusted survival curves were used to compute log[−log(survival)]; (2) a time dependent factor was modeled in a separate Cox analysis; and (3) the primary Cox model was re-estimated with all patients censored at one year of follow-up, with subsequent follow-up treated as a separate observation. This final model was stratified using a binary variable that identified observations for CAPD patients treated more than one year. The same binary variable was then included as a covariate in the proportional hazards model to isolate mortality effects observed for CAPD patients after one year of follow-up.

Several supplementary proportional hazards models were considered in sensitivity analyses. Two separate models for diabetic patients included covariates measuring the duration and severity of diabetes as reported on the data abstraction form [8]. The first model included a covariate for the duration of diabetes in years prior to onset of ESRD, with adjustment for pre-treatment risk factors. A separate model, also for diabetic patients only, included a covariate for patients with a prior history of diabetes but with a diagnosis other than diabetes identified as the primary cause of ESRD.

An alternate proportional hazards specification included a covariate for undernourished patients to measure effects of nutrition on mortality, independent of serum albumin and serum creatinine. A third set of models analyzed the interaction between age and treatment modality by examining the relative mortality risk for CAPD compared to HD separately for two broadly defined groups of younger and older patients (<50, ≥50 years at ESRD onset). An additional set of proportional hazards models evaluated CAPD and HD mortality risk without assuming proportionality in the hazard functions for CAPD and HD over time. This set of models was designed to test the null hypothesis that the relative risk of death for CAPD relative to HD was not different in the short term (that is, first year of treatment) from the longer term (after the first year of treatment).

Table 2. Relative chance[a] of selected comorbid conditions being present at onset of ESRD for CAPD compared to HD, with adjustment for age and diabetes, 1986 to 1987 incident Medicare patients (N = 4,057)

Comorbid condition at onset of ESRD	Unadjusted % *Present*	Relative chance, adjusted[b]		
		Hemodialysis (*reference*)	CAPD	
			Relative chance	P[c]
Congestive heart failure	40.3	1.00	0.92	0.09
Coronary heart disease[d]	40.4	1.00	0.97	0.49
Cerebrovascular accident	10.1	1.00	0.75	0.03
Peripheral vascular disease (PVD)[e]	19.3	1.00	1.23	<0.01
Amputation due to PVD	4.6	1.00	0.74	0.13
Unable to walk independently	2.3	1.00	0.56	<0.01

[a] Analysis excludes patients treated with CCPD and differs slightly from previous results for CAPD/CCPD in reference 2
[b] Adjusted for age and diabetes
[c] The statistical significance of relative risk values comparing CAPD to HD was estimated using Cochran-Mantel-Haenszel statistics
[d] Includes coronary heart disease, bypass surgery, coronary angioplasty, and abnormal angiograph
[e] Includes amputation due to PVD, absent foot pulses, and claudication

Results

Sample description

Table 1 indicates that patients selected for HD were on average older and more likely black and non-diabetic than patients selected for CAPD. When adjusting for the two major factors of age and diabetes status, CAPD patients (relative to HD patients) were less likely to have a cerebrovascular accident and were more likely to have peripheral vascular disease and to be ambulating independently (Table 2). Patients receiving a first kidney transplant during the follow-up period were 9 and 7% for diabetic CAPD and HD patients, respectively, and 8 and 11% for non-diabetic CAPD and HD patients.

Relative mortality risk

Adjusted relative mortality risks associated with selected patient characteristics, including comorbid conditions, are reported separately in Table 3 for 1,725 diabetic and 2,411 non-diabetic patients. For each patient characteristic, mortality estimates are expressed relative to a selected reference group, which is assigned a mortality risk of 1.00; any deviation from 1.00 suggests an estimated relative risk (RR) that is increased (if RR > 1.00) or reduced (if RR < 1.00) compared to the reference group. Across diabetic and non-diabetic subgroups in Table 3, evidence of a reduced mortality risk, on average, was observed for females (RR = 0.88 and 0.76, that is 12 and 24% lower mortality than males), for blacks (36 and 15% lower mortality than whites), and for younger patients (2 and 5% increase in mortality per year of age). Among all patients with a history of diabetes, statistically significant elevated mortality risks were associated with the presence of coronary heart disease (RR = 1.20, P = 0.02), congestive heart failure (RR = 1.31, P < 0.01),

Table 3. Proportional hazards, mortality estimates for patient risk factors by presence of diabetes at onset of ESRD, 1986 to 1987 incident Medicare dialysis patients

Risk factor at onset of ESRD	Risk group	Reference	Diabetic (N = 1,725) Relative risk	Diabetic (N = 1,725) P	Non-diabetic (N = 2,411) Relative risk	Non-diabetic (N = 2,411) P
Gender	Female	Male	0.88	0.10	0.76	<0.01[a]
Age at ESRD	Age 68.7	Age 58.7	1.24	<0.01[a]	1.55	<0.01[a]
Race (at age 58.7)	Black	White	0.64	<0.01[a]	0.85	0.10
	Other	White	0.81	0.16	0.71	0.11
Race*age	Black*68.7	White*68.7	0.64	0.97[c]	0.73	0.02[c]
Modality (at age 58.7)	CAPD	HD	1.26	0.03	0.84	0.25
	CCPD	HD	1.06	0.82	0.96	0.92
Modality*age	CAPD*68.7	HD*68.7	1.45[b]	0.11[c]	0.95	0.20[c]
Coronary heart disease	Present	Absent	1.20	0.02	1.11	0.19
Congestive heart failure	Present	Absent	1.31	<0.01	1.23	<0.01
Cerebrovascular accident	Present	Absent	1.16	0.14	1.35	<0.01
Peripheral vascular disease	Present	Absent	1.23	<0.01	1.08	0.46
Neoplasm	Present	Absent	1.14	0.32	1.62	<0.01[a]
Serum albumin *g/dl*	≤2.5	3.6–4.0	2.27	<0.01[a]	2.07	<0.01[a]
	2.6–3.0	3.6–4.0	1.34	<0.01[a]	1.66	<0.01[a]
	3.1–3.5	3.6–4.0	1.36	<0.01[a]	1.18	0.05
	>4.0	3.6–4.0	1.00	0.99	0.85	0.25
Smoking status: active, or past history (time unknown)	Yes	No	1.22	0.06	1.31	<0.01
Obese	Yes	No	0.95	0.53	0.77	0.03
Physical abilities						
Independent ambulating	Unable	Able	1.20	0.22	0.93	0.65
Independent eating	Unable	Able	1.07	0.73	1.25	0.34
Independent transferring	Unable	Able	1.15	0.36	1.12	0.49
Pre-dialysis BUN *mg/dl*	80	60	1.00	0.94	0.98	0.47
Pre-dialysis serum creatinine *mg/dl*	6	9	0.86	<0.01[a]	0.91	<0.01
Systolic blood pressure *mm Hg*	<120	120–159	1.13	0.37	1.54	<0.01[a]
	160–199	120–159	0.81	<0.01	1.19	0.04
	≥200	120–159	1.05	0.74	1.02	0.92
Missing case mix data	Yes	No	0.97	0.79	1.01	0.93

[a] $P < 0.001$

[b] A white diabetic patient (68.7 years of age) receiving CAPD would have a relative risk of 1.45 compared to a white diabetic patient (68.7 years of age) on HD. This RR is the product of 1.15*1.26 (interaction RR = 1.15 per 10 years).

[c] P value for interaction with age

and peripheral vascular disease (RR = 1.23, P = 0.01). In a separate analysis (not presented), lower adjusted mortality was associated with patients indicating a history of diabetes but with another medical condition identified as the primary cause of ESRD (RR = 0.80, $P < 0.01$) when compared to patients whose primary cause of ESRD was diabetes.

Among non-diabetic patients, statistically significant elevated mortality risks were associated with congestive heart failure (RR = 1.23, $P < 0.01$), CVA (RR = 1.35, $P < 0.01$), neoplasm (RR = 1.62, $P < 0.01$), and smoking (RR = 1.31, $P < 0.01$). As with diabetic patients, statistically significant ($P < 0.05$) adverse results were associated with serum albumin levels below 3.5 g/dl for non-diabetic patients (≤2.5 g/dl, RR = 2.07; 2.6 to 3.0 g/dl, RR = 1.66; 3.1 to 3.5 g/dl, RR = 1.18). In an alternative model for non-diabetics only, an indicator of undernourished predicted higher mortality (RR = 1.42, $P < 0.01$) when excluding serum albumin and creatinine from the same proportional hazards model. Analyses for diabetic and non-diabetic patients combined (not presented) indicated that serum albumin levels less than 3.5 g/dl were predictive of higher mortality in both CAPD and HD patients ($P < 0.01$) and may have a steeper risk gradient in CAPD patients than in HD patients; (≤2.5 g/dl, RR = 2.82 vs. RR = 2.10) and (2.5 to 3.0 g/dl, RR = 2.36 vs. RR = 1.38).

With adjustment for patient risk factors, the relative mortality risk for CAPD among non-diabetics was 0.84 (that is, reduced by 16%) compared to HD at the mean age (58.7 years) of all HD patients, although this result was not statistically significant (P = 0.25). Conversely, the selection-adjusted mortality of CAPD patients was 26% higher overall (RR = 1.26) and statistically significant (P = 0.03) among diabetic patients at age 58.7. This adjusted relative risk translated to an annual absolute mortality of approximately 27% for diabetic HD patients and 34% for diabetic CAPD patients. Analysis of the interaction of age with treatment modality (RR = 1.01 per year, P = 0.11) yielded a statistically insignificant result that may indicate elevated mortality risk for CAPD compared to HD that is accentuated in older diabetic patients. The magnitude of this effect, if not due to random variation, translated to statistically significant elevated mortality for CAPD compared to HD among diabetic patients who were 58 years of age at onset of ESRD (RR = 1.25, $P < 0.05$) and 63 years of age (RR = 1.34, $P < 0.01$), and for older ages. No statistically significant difference was found in mortality between the modality groups

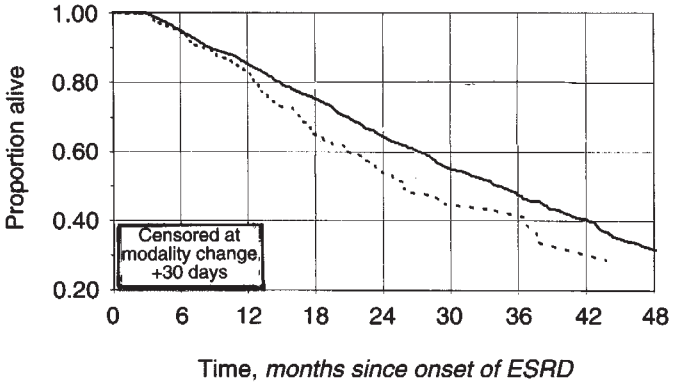

Fig. 1. *Proportional hazards estimates of patient survival for CAPD (– – –, N = 310) and HD (——, N = 1,379), incident Medicare patients, 1986–1987.* Diabetic patients only. Includes (a) patients with diabetes as primary cause of ESRD, and (b) patients with a history of diabetes within ten years prior to onset of ESRD but with another reported primary cause of ESRD. Survival probabilities were calculated for the mean of each of the following characteristics: age; race; sex; and mix of comorbid conditions reported in Table 3. Patients surviving <90 days were excluded. Sample size for CAPD and HD, respectively, at one-year follow-up intervals: onset of ESRD, 310, 1379; one year, 177, 994; two years, 63, 626; three years, 27, 247.

for diabetic patients less than 58 years of age at onset of ESRD ($P > 0.05$).

Selection-adjusted patient survival

Stratified CAPD and HD survival curves, estimated using the Cox proportional hazards model and adjusted for the pre-treatment risk factors described in Table 3, are presented in Figure 1 for diabetic patients and in Figure 2 for non-diabetic patients. Survival probabilities were calculated for the average patient mix, that is, for the average age, race, sex, and mix of comorbid factors presented in Table 3. Among non-diabetic patients, adjusted survival estimates were overall very similar for CAPD and HD at one year (91.8 and 90.6%, respectively), two years (78.0 and 78.4%), and through approximately 3.5 years of follow-up. Among diabetic patients, survival was similar for CAPD and HD at one year (83.3% and 85.4%, respectively), but was reduced for CAPD relative to HD at two years (54.0% compared to 64.6% for HD) and through the remainder of the follow-up period. Proportionality between the hazard functions for CAPD and HD was evaluated using graphical techniques, by specifying a time dependent covariate in a proportional hazards model, and by including a covariate in the primary model to detect elevated mortality for CAPD after one year of follow-up. None of these statistical tests identified a non-proportionality effect for CAPD on diabetic patient mortality, indicating that the proportional hazards model was appropriate for these analyses.

Sensitivity analyses

In a separate analysis, not shown, patient mortality was examined using an intent-to-treat model, which classified a patient's dialysis modality at one month following ESRD onset but did not censor at a change in dialysis modality [14]. Under this alternative specification, the estimated relative mortality risks for CAPD compared to HD were not materially changed from the modality history specification presented above. A recent report from the Michigan Kidney Registry agrees with the observation that comparisons of CAPD and HD yield similar results when using a modality history versus an intent-to-treat assignment of modality [14].

Separate tests were performed on the hypothesis that findings of higher relative mortality for CAPD among diabetic patients were confined to a broadly defined group of older patients whose diabetes was almost exclusively identified as type II (NIDDM) [15]. Two distinct proportional hazards models, one for younger (age <50 years) and one for older (age ≥50 years) diabetic patients, were specified to test this hypothesis. The relative mortality risk for older CAPD patients ($N = 1,312$) was 1.34 ($P = 0.02$), while younger CAPD patients ($N = 413$) were found to have a relative risk of 1.11, a result that was not statistically different from the reference group of younger HD patients ($P = 0.68$). Based on the standard errors for the CAPD relative risk estimates, the relative mortality (CAPD relative to HD) for the two diabetic age groups was not statistically different from each other (1.34 was not statistically different than 1.11).

A third set of mortality analyses considered the validity of assigning patients with information missing for indicators of comorbidity to the reference group defined in each case. When supplementing proportional hazards models with covariates identifying missing information for each comorbid condition, no statistically significant association of mortality with "missing information" covariates was established relative to the reference value, for any of the conditions. Relative risk estimates for each comorbid condition were not materially changed by the method described earlier of assigning missing values to the mean (for numeric variables) or by regarding the comorbid condition as not present when medical records did not indicate whether the condition was present or absent.

Discussion

The selection of 1986 to 1987 incident ESRD patients for CAPD and for HD varied according to patient characteristics, including comorbid conditions present at onset of ESRD, that were associated with elevated mortality risks. Using estimates of the relative mortality risk for age, race, and diabetes reported previously [9–12] and differences in the selection of patients for CAPD versus HD reported in Table 1, the pre-treatment risk for CAPD patients compared to HD patients was evaluated. The unadjusted death rate for HD patients would be expected to be increased by 18% due to age, while the unadjusted death rate for CAPD patients would be expected to be increased by 3% and 2% due to diabetes and race, respectively. The approximate net effect of differences in age, diabetes, and race was 13% greater expected mortality risk among patients selected for HD compared to CAPD, largely because of the on average five-year age differential between the two treatment groups. The increased mortality risk associated with several comorbid conditions [7] which were found to be more likely present among HD patients (Table 2) provides further evidence of higher mortality risk at onset of ESRD for patients selected for HD.

The statistical adjustments made in the current analyses account for the simultaneous mortality effects of all reported risk factors. Non-diabetic patients treated with HD revealed similar adjusted survival outcomes as non-diabetic patients treated with CAPD. This finding is consistent with reports from

Spain [4], while Serkes et al [5] reported results of borderline statistical significance (RR = 0.62 for CAPD vs. HD, $P = 0.08$). In contrast, adjusted mortality comparisons among diabetic dialysis patients in the current study revealed higher mortality risk for CAPD patients compared to HD patients (RR = 1.26, $P = 0.03$). Maiorca et al [3] reported a similar elevated mortality risk for all (that is, diabetic and non-diabetic patients combined) CAPD compared to all HD patients (RR = 1.35) at the mean age of 53 years, although statistical significance was not established ($P = 0.16$).

The proportional hazards analysis presented in Table 3 contains a statistically insignificant age and modality interaction effect ($P = 0.11$ and $P = 0.20$ for diabetic and non-diabetic patients, respectively) that corresponds with the specification used by Maiorca et al [3]. Specification of this interaction term is also consistent with findings from the USRDS of higher survival for younger incident diabetic patients receiving CAPD compared to HD and lower survival for older incident diabetic patients receiving CAPD [1]. Univariate findings of an age effect on mortality comparisons between CAPD and HD were found to be particularly strong among prevalent diabetic patients, with the crossover in CAPD and HD mortality occurring between 40 and 50 years of age [1]. Maiorca et al [3] also identified patterns in mortality between age and treatment modality, although results indicated worse outcomes for older patients receiving HD as opposed to CAPD, possibly due to different patterns of selection between Italy and the U.S. [2].

Results from proportional hazards tests in the current study indicate an adverse though overall statistically insignificant effect of increasing age on the relative mortality for CAPD compared to HD among diabetic patients. Diabetic ESRD consists of two entities (type I, or IDDM; and type II, or NIDDM) which identify patients by age, with some overlap. Cowie et al [15] showed that despite some overlap, age at onset of ESRD permits a classification of diabetic ESRD since diabetic patients over age 50 in the U.S. have almost exclusively type II diabetes. Proportional hazards analyses comparing adjusted mortality separately for two broadly defined age groups (<50 years, ≥50 years) of diabetics suggest that elevated mortality for CAPD relative to HD may be accentuated among older patients. Elevated CAPD mortality associated with increasing age among diabetics (Table 3), if not occurring by chance, indicates that the relative risk of death is statistically different by treatment modality among patients 58 years and older (adverse for CAPD compared to HD). The interaction effect in Table 3 indicates that adjusted mortality for CAPD and HD intersected between 40 and 45 years of age, consistent with previous USRDS mortality analyses for both incident and prevalent diabetic patients [1].

Thus the present analysis appears to agree with findings from Michigan [14] that young diabetic patients treated with CAPD may have a lower mortality risk than corresponding hemodialysis patients. Results from comparative studies that do not adjust for comorbid conditions [1, 14] may, however, overstate differences among young diabetic patients according to a recent USRDS report [2]. This study showed that among diabetics, younger CAPD patients had a statistically significant lower count of comorbid conditions than younger HD patients. Thus the selection of younger diabetic patients with fewer comorbid conditions to CAPD rather than to HD therapy would partially

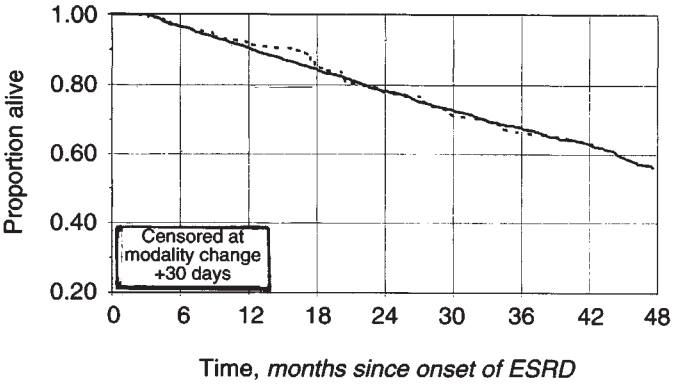

Fig. 2. *Proportional hazards estimates of patient survival for CAPD (– – –, N = 371) and HD (——, 1,997), incident Medicare patients, 1986 to 1987.* Non-diabetic patients only. Survival probabilities were calculated for the mean of each of the following characteristics: age; race; sex; and mix of comorbid conditions reported in Table 3. Patients surviving <90 days were excluded. Sample size for CAPD and HD, respectively, at one-year follow-up intervals: onset of ESRD, 371, 1997; one year, 224, 1455; two years, 109, 995; three years, 55, 471.

explain previous findings of lower mortality for younger CAPD patients when only limited adjustments were made [1, 14]. The present study suggests that a reversal of results may occur for diabetic patients at young ages, although statistical significance was not observed.

Proportional hazards estimates of diabetic patient survival adjusted for pre-treatment risk factors (Fig. 1) indicated worse outcomes for CAPD after one year of therapy, an observation that may not be detected in studies restricted to one year of follow-up. Outcomes were similar for diabetic CAPD and HD patients during the first 12 months of treatment, but the observed higher death rates for CAPD between 12 and 18 months following onset of ESRD led to lower survival estimates for CAPD compared to HD during the remainder of the follow-up period. Tests of proportionality between the hazard functions for CAPD and HD indicated no statistically significant difference between adjusted CAPD survival in the short term and the longer term. Results from two additional proportional hazards models (not presented) for diabetic patients indicated that adjusted CAPD mortality was higher after the first year of ESRD treatment (RR = 1.34, $P = 0.04$) than mortality observed from 90 days to one year following first ESRD treatment (RR = 1.14, $P = 0.47$), but was not statistically different. Tests of the divergence in survival between CAPD and HD indicate that the null hypothesis, that is, that the relative mortality risk for CAPD varies over time due to random variation, cannot be statistically rejected.

Analyses of diabetic patient mortality were also repeated with an adjustment for the duration of diabetes (in years) prior to onset of ESRD. No statistically significant evidence of an association of duration of diabetes with mortality was found (RR = 1.01 per year with diabetes, $P = 0.32$), possibly because comorbidity that increases with duration of diabetes was adjusted in this analysis. A lower mortality risk was estimated for the subgroup of patients with a history of diabetes but with another identified cause of ESRD (RR = 0.80, $P < 0.01$) compared to patients with diabetes as the primary diagnosis. Results for this subgroup of diabetic patients, which represents approximately 20 to 30 percent of all patients with a history of

diabetes (note distribution in Table 1), suggest the need for further study of the severity of diabetes at onset of ESRD for patients with and without diabetes as the primary diagnosis. These additional adjustments for the duration and severity of diabetes at the initiation of renal replacement therapy did not materially affect comparisons of CAPD with HD in the short or longer term.

The graphical pattern of diverging CAPD and HD survival curves after one year of ESRD treatment can be seen for diabetic and non-diabetic patients combined in at least two recent studies [3, 4]. The relatively high mortality risk for diabetic CAPD patients after the first year of therapy suggests that the protective effect of residual renal function may be lost in CAPD patients at this stage, while HD patients may have lost their renal function earlier during the first year [16]. Thus, inadequate dialysis treatment may play a greater role after the first year of CAPD. However, this speculation would assume that HD patients received adequate dialysis despite their earlier loss of residual function. Previous analyses from the USRDS Case Mix Severity Special Study indicated no statistically significant relationship between prescribed Kt/V and mortality ($P > 0.10$). At least one recent national study has suggested that inadequate therapy may be responsible for relatively high mortality among HD patients [17]. The same may be true for peritoneal dialysis patients even with good peritoneal equilibration test results, if a large fraction of CAPD patients would utilize fewer exchanges than prescribed. If underdelivery of dialysis caused higher mortality for HD and CAPD, proper adjustment for the delivered dose of dialysis would likely lower mortality for HD and CAPD. Any existing differences in the adequacy of delivered dialysis between CAPD and HD may have affected survival comparisons reported here.

As an alternative explanation, one may consider the role of unmeasured predictors of outcome at the start of ESRD. However, mortality risks associated with pre-existing comorbid conditions of a type or severity that is unmeasured by this analysis would be expected to have an early rather than late impact on survival. Clearly, further research will be required to substantiate current findings and to assess the reasons for an apparent divergence in survival between CAPD and HD among diabetic patients.

The current analyses, based on a historical prospective national study of case mix severity and patient mortality, cannot assign a cause-and-effect relationship to these observational data. Mortality comparisons should be viewed with caution since other unmeasured comorbid factors as well as the unmeasured severity of reported comorbid factors may not be distributed evenly between the two treatment groups. Whether current evidence of higher overall mortality for CAPD relative to HD among patients with diabetes is a consequence of the CAPD therapy itself, unmeasured patient selection, residual renal function, or adequacy of delivered dialysis among incident diabetic patients will therefore require further study. Adjusted survival outcomes for non-diabetic patients treated with HD and CAPD were similar in this large national study.

Acknowledgments

The United States Renal Data System and this study are supported by contract NIH NO 1-DK-8-2234 and 3-2202 from the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland, USA. The support of the United States Renal Data System Scientific Advisory Committee, the cooperation of the Health Care Financing Administration, and the entry of quality data by the end-stage renal disease Networks are gratefully acknowledged.

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